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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,004	09/25/2003	Kazuhiro Aikawa	Q77153	6236

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

MAIL DATE	DELIVERY MODE
09/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,004	AIKAWA, KAZUHIRO	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 8-2-07 is acknowledged.

Claims included in the prosecution are 1 and 4-6.

In view of the amendments, the 112 rejections are withdrawn.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1 and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 583 665 of record.

EP discloses liposomes containing claimed benzimidazole derivatives. The phospholipids used are PC and PS in a molar ratio of 1:1. The liposomes and the active agents are added to the culture plates and therefore, in the absence of showing otherwise, that the compounds are either loaded into the liposomes or adsorbed to the liposomes meeting the requirements of instant claims (abstract and page 33).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that EP fails to disclose preparing the liposomes so that the liposome contains the benzimidazole compounds thereof and that the pharmaceutical test discloses that the test compounds and liposomes are added separately to the cultures of macrophages. Applicant argues that there are significant differences between WO 560 and EP 665 such that the method disclosed in WO 560

does not necessarily guarantee that a mixture of benzimidazole compounds and liposomes would result in the liposomes incorporating the benzimidazole compounds. Applicant further argues that that their experiments comparing the liposomes disclosed in WO 560 show that liposomes cannot incorporate the claimed benzimidazole. This argument is not persuasive for the following reason. The examiner has only cited the reference of WO, which shows that a compound can be associated with liposomes when the liposomes are incubated with the active agents. The rejection however, is based on EP reference and the rejection is a 102 rejection. Therefore, applicant is required to show that the product in EP and not that in WO is different from instant product. Applicant has not shown that the benzimidazole in EP is not associated with the liposome membrane under the incubation conditions.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0583 665 cited above in view of Aikawa (7,101,532) or Kitaguchi (7,008,614) or Schmidt (6,077,529) individually or in combination.

EP as discussed above teaches liposomes containing PC and PS in 1:1 molar

ratio. The benzimidazole however, is added to the medium containing the liposomes. According to EP the benzimidazole derivatives are for the treatment of hyperlipidemia and arteriosclerosis.

Aikawa, and Kitaguchi while disclosing liposomal compositions for radiography of a vascular disease (atherosclerosis) teach that liposomes are selectively taken up by vascular smooth muscle cells and macrophages. The liposomes contain PC and PS in 1:1 molar ratio (abstract, Examples 5, 68 and 9 of Aikawa; abstract, Examples 4, 5 and 8 of Kitaguchi).

Schmidt discloses that liposomes containing are useful in handling arteriosclerosis. The phospholipids, which could be used in making the liposomes, include PC and PS (abstract, col. 5, lines 24-34 and claim 4).

Assuming that the benzimidazole derivatives of EP are not associated with the liposomal membrane: it would have been obvious to one of ordinary skill in the art to encapsulate or associate the benzimidazole derivatives of EP in liposomes since the references of Kitaguchi, and Aikawa each teach that the liposomes are selectively taken up by vascular smooth muscle cells and macrophages and since the reference of Schmidt teaches that liposomes can be used in handling atherosclerosis.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that both Aikawa, and Kitaguchi teach compounds which are contrast agents and have no pharmacological activity and they do not t each or suggest using the liposomes thereof to exhibit any pharmacological activity. Applicant argues that Schmidt discloses producing asymmetrical liposomes to handle

arteriosclerosis and thus extract cholesterol. These arguments are not persuasive. Whether it is a contrast agent or pharmacological agent, the references of Aikawa, and Kitaguchi show that hydrophobic compounds can be encapsulated within the liposomes. These references also show that such liposomes are selectively taken up by vascular smooth muscle cells and macrophages. Therefore, one of ordinary skill in the art would expect irrespective of the nature of the encapsulated compound (contrast agent or a drug) the liposomes to reach the vascular tissue and macrophages (see Supreme court decision in KSR International Co. V. Teleflex Inc., 550 U.S. -, 82 USPQ2d 1385 (2007). With regard to applicant's arguments pertaining to Schmidt, the examiner points out that this reference is combined to show that the ability of the liposomes containing PC and PS to reach the vascular tissue, whether the purpose is to extract cholesterol or not.

5. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aikawa (5,387,600) of record in view of Aikawa (7,101,532) or Kitaguchi (7,008,614) or Schmidt (6,077,529) individually or in combination.

Aikawa (600) teaches that benzimidazole derivatives for the treatment of atherosclerosis (abstract and claims). What is lacking in Aikawa is the use of liposomes as the carriers.

Aikawa, and Kitaguchi while disclosing liposomal compositions for radiography of a vascular disease (atherosclerosis) teach that liposomes are selectively taken up by vascular smooth muscle cells and macrophages. The liposomes contain PC and PS in 1:1 molar ratio (abstract, Examples 5, 68 and 9 of Aikawa; abstract, Examples 4, 5 and 8 of Kitaguchi).

Schmidt discloses that liposomes containing are useful in handling arteriosclerosis. The phospholipids, which could be used in making the liposomes, include PC and PS (abstract, col. 5, lines 24-34 and claim 4).

It would have been obvious to one of ordinary skill in the art to encapsulate or associate the benzimidazole derivatives of Aikawa (600) in liposomes since the references of Kitaguchi, and Aikawa each teach that the liposomes are selectively taken up by vascular smooth muscle cells and macrophages and since the reference of Schmidt teaches that liposomes can be used in handling atherosclerosis.

Applicant provides no specific arguments with regard to this rejection. The rejection therefore, is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK